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EXAMINER	
ALSTRUM ACEVEDO, JAMES HENRY	
ART UNIT	PAPER NUMBER
1616	

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12/09/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/723,626	PRATT ET AL.	
	Examiner	Art Unit	
	JAMES H. ALSTRUM ACEVEDO	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 November 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-31,39-50 and 52-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-31,39-45,47-50 and 52-54* is/are rejected.

7)☒ Claim(s) *46* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/10/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 22-31, 39-50, and 52-54 are pending. Applicants previously cancelled claim 1-3, 4-21, and 32-38. Claim 51 is newly cancelled. Claims 53-54 are new. Receipt and consideration of Applicants' amended claim set, new IDS, 1.132 declaration (i.e. "Dr. Jarrett declaration") and remarks/arguments submitted on November 10, 2009 are acknowledged. All rejections/objections not explicitly maintained in the instant office action have been withdrawn per Applicants' claim amendments.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/10/2009 has been entered.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 42-43 **remain rejected** under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 42-43 are vague and indefinite because these claims claim a range of specific gravity of "greater than about 1.0063" and "less than about 1.0063," respectively. The term "about" is not defined by Applicants' specification. An ordinary skilled artisan would be unable to ascertain the metes and bounds of the recited specific gravity ranges because the minimum or maximum endpoint cannot be unambiguously determined. As a result the ordinary skilled artisan would be forced to guess at the possible meaning intended by the term about as well as what was the actual specific gravity range required by claims 42-43.

Response to Arguments

Applicant's arguments filed November 10, 2009 have been fully considered but they are not persuasive. Applicants traverse the instant rejection by referring to MPEP § 2173.05(b) and arguing that the ordinary skilled artisan would understand the meaning of about when referring to the specific gravity of the CSF, which is known to vary slightly between individuals.

The Examiner respectfully disagrees with Applicants' arguments, which demonstrate a misunderstanding of the basis of the rejection. The instant rejection is not merely based on the argument that "about" in isolation is indefinite, but rather on the context in which the about "about" is used. In the rejected claims the indefinite results from the ambiguity of the recited specific gravity ranges that recite "***greater than about***" or "***less than about***." It is the combination of about with the terms "greater than" and "less than" that is the source of the problem, because it renders the required ranges ambiguous. The ordinary skilled artisan is unable to ascertain the metes and bounds of the recited ranges as the maximum or minimum

endpoint of the recited ranges is uncertain. Thus, Applicants' arguments are unpersuasive. The rejection is maintained.

Consideration of Dr. Jarrett's 1.132 Declaration

Dr. Jarrett's opinion declaration indicates that he believes Applicants' invention is non-obvious per the teachings of Soon-Shiong (U. S. Patent No. 5,560,933). Specifically, Dr. Jarrett indicates that Applicants' specification describes an invention that is non-obvious because (1) Soon-Shiong does not explicitly teach the explicit use of buoyancy agents or contemplate modulating the specific gravity of compositions; (2) Dr. Jarrett believes that it would not have been obvious to use Soon-Shiong's invention to administer therapeutic agents to the CSF; (3) Dr. Jarrett believes Soon-Shiong's invented compositions would be ineffective to deliver therapeutic agents to a specific target in the CSF, because either the dispersion medium would dissolve in the CSF or form liquid droplets causing the active agent to be release into the CSF as either a liquid in solution or a solid mass; and (4) solid therapeutic agents upon release would move about the CSF according to the density of the active agent and liquid active agents would disperse in the CSF as coalesced separate liquid phases or dissolve (if soluble).

The Examiner respectfully disagrees with Dr. Jarrett's opinions and conclusions, because Dr. Jarrett's comments do not address Applicants' claims, but rather his reading of Applicants' specification. Furthermore, Applicants' claims either do not recite a specific gravity value (e.g. claims 22-31, 39-41, 44-50, and 52-54) or collectively contemplate specific gravity values encompassing the entire universe of possible values (i.e. specific gravity values greater than 1.0063 as well as values less than 1.0063) (i.e. claims 42-43). Almost every composition will

necessarily exhibit a specific gravity that is either greater than 1.0063 or less than 1.0063, with the remainder of possible compositions exhibiting a specific gravity value of 1.0063. Regarding the intended use of the dispersion medium in Soon-Shiong, this observation is irrelevant, because Soon-Shiong explicitly teaches that particles containing active agent (e.g. Vitamin E) (e.g. col. 5, line 65 through col. 6, line 3) in the core may also contain dispersing agent (e.g. water, saline, vegetable oil, soybean oil, etc.) (col. 6, line 47 through col. 7, line15 and col. 9, lines 3-7) and that these compositions can be administered intrathecally (i.e. into the CSF) (col. 4, lines 28-31). Thus, Soon-Shiong's teachings effectively teach administration of substantially similar particles via the same rout of administration (i.e. intrathecally into the CSF). Therefore, Dr. Jarrett's opinion declaration, upon consideration, is found unpersuasive.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 22-30, 40-45, 47-50, and 52-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Soon-Shiong et al. (U.S. Patent No. 5,560,933) ("Soon-Shiong") in view of Kim et al. (WO 94/26250) (New IDS reference) and Harris, D.C. ("Quantitative Chemical Analysis, 4th ed., W. H. Freeman and Co.: 1995, pp 26).

Applicant Claims

Applicants claim (1) a method of administering a therapeutic agent within the central nervous system (CNS) comprising intrathecal administration of a composition to a subject's CNS, wherein said composition comprises a biodegradable polymer having a therapeutic agent and a buoyancy agent contained therein, wherein the buoyancy agent is selected from gases and oils and is controllably buoyant within the CSF.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

Soon-Shiong teaches methods for in-vivo delivery (e.g. intrathecal administration) of substantially water insoluble pharmacologically active agents (e.g. taxol) and compositions useful thereof (title; abstract; col. 3, lines 24-29; and col. 4, lines 28-33). Soon-Shiong's

invented compositions comprise particles of substantially water insoluble active agents contained within a shell having a cross-sectional diameter of no greater than 10 microns, wherein a cross-sectional diameter of less than 1 micron is most preferred (col. 5, lines 23-30). Suitable active agents for incorporation into Soon-Shiong's invented compositions include **aspirin, ibuprofen, estrogen (i.e. a hormone), prednisolone, cortisone, hydrocortisone, anesthetics, immunosuppressive agents**, and preferably **taxol (i.e. a cytotoxic agent)** (col. 5, lines 31-56). The invented composition may also contain nutritional agents within the shell, such as **amino acids**, sugars, **proteins, carbohydrates**, **fat-soluble vitamins, such as vitamins A,D, E, and K**, and combinations thereof (col. 5, line 65 through col. 6, line 3). **Amino acids, sugars, proteins, carbohydrates, and vitamins A, E, and K read on active agents that are "other plant products".** The shell of Soon-Shiong's invented particles can be made of any natural or synthetic biocompatible polymer that may be cross-linked via the formation of disulfide linkages, such as **proteins** (e.g. **albumin, insulin, hemoglobin, immunoglobulins, fibronectin, fibrinogen,** etc.), **oligopeptides, polysaccharides** (e.g. starch, cellulose, chitin, dextrans, etc.), and synthetic polymers, which are amenable to chemical functionalization to introduce sulfhydryl moieties, such as polyvinyl alcohol, **polyhydroxyethyl methacrylate**, polyacrylic acid, polyacrylamide, polyvinyl pyrrolidone, etc.

Soon-Shiong teaches that optionally in the preparation of the compositions dispersing agents in which the active agent is dissolved or suspended may also be included, such as **vegetable oils (e.g. soybean oil, coconut oil, olive oil safflower oil, cotton seed oil, and the like**), aliphatic, cycloaliphatic, or aromatic hydrocarbons having 4-30 carbon atoms, aliphatic or aromatic alcohols, esters, ethers, and alkyl or aryl halides, all having 2-30 carbon atoms are

indicated as being suitable dispersing agents (col. 6, lines 47 through col. 7, line 4). The invented particles with a biocompatible shell and an active agent contained therein are typically **delivered as a suspension in a biocompatible aqueous liquid** (col. 7, lines 15-22). In the preparation of Soon-Shiong's invented compositions, it is contemplated that **the particle shells contain therein both the substantially water insoluble active agent dissolved or suspended in the dispersing agent** (col. 8, line 65 through col. 9, line 7). In Example 2 (col. 11, lines 12-35), Soon-Shiong teaches **an albumin protein shell containing soybean oil**. Shells comprising **a mixture of albumin and PEG-thiol** with a molecular weight of 2,000 g/mol are also exemplified in Example 11, col. 16, lines 20-55). The inclusion of PEG is art-recognized as increasing protein/enzyme in vivo circulation time and is expected to prolong drug release in vivo (col. 9, lines 38)

Kim teaches the **administration of therapeutic agents to the CSF to treat neurological disorders** by administration of **dispersion systems having a higher specific gravity than the CSF** (i.e. hyperbaric compositions), such as compositions comprising encapsulated iohexol, iodixanol, metrzamide, carbohydrates, etc. as well as **hypobaric dispersion systems (i.e. having a lower specific gravity than the CSF)** (title; abstract; claims 1 and 31-37).

Harris teaches that the **density of air at 25 °C and 1 atm of pressure is 0.012 g/ml**. Therefore, the specific gravity of air at 25 °C and 1 atm of pressure is approximately 0.012. Air is a mixture of nitrogen, oxygen, and other gases.

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Soon-Shiong does not exemplify a method of administering a therapeutic agent by intrathecal administration. This method, however, is suggested per the teachings of Soon-Shiong. Soon-Shiong does not explicitly teach the inclusion of buoyancy agents. This deficiency is nonetheless obvious per Soon-Shiong's teachings and is also explicitly taught by Kim. Soon-Shiong does not teach a buoyancy agent that is a gas or a mixture of oxygen and nitrogen (e.g. air). This deficiency is cured by the combined teachings of Kim and Harris.

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been prima facie obvious at the time of Applicants' invention to utilize the invented particles to administer an active pharmaceutical agent intrathecally, because Soon-Shiong explicitly teaches that the invented compositions are suitable for the in vivo administration of active substances and defines in vivo delivery to include intrathecal administration. Soon-Shiong does not explicitly teach the inclusion of buoyancy agents, however, Soon-Shiong's invented particles may comprise a dispersing agent, such as vegetable oils, which Applicants' admit are suitable buoyancy agents. Thus, Soon-Shiong's teachings suggest the administration of biocompatible aqueous suspensions of particles comprising (i) a biocompatible shell, such as cross-linked albumin, which is also biodegradable, and (ii) a substantially water insoluble active agent dissolved or suspended in a dispersing agent, such as soybean oil, which is necessarily a buoyancy agent, as admitted by Applicants. An ordinary skilled artisan would have been motivated to administer Soon-Shiong's compositions intrathecally and would have had a reasonable expectation of success in intrathecally administering these compositions, because Soon-Shiong's compositions are taught as being

suitable for intrathecal administration. Regarding the intrathecal administration of Soon-Shiong's compositions to patients diagnosed with a central nervous system disorder, the preferred active agent in Soon-Shiong's compositions is a taxol, which is a well-known anticancer agent.

It would have been prima facie obvious to include a buoyancy agent in Soon-Shiong's compositions, because Kim teaches the incorporation of materials having a specific gravity higher (i.e. hyperbaric) or lower (i.e. hypobaric into the dispersions systems to affect targeted delivery within the CSF. An ordinary skilled artisan would have been motivated to combine the teachings of Soon-Shiong and Kim, because both references teach the intrathecal administration of active agents. Regarding the identification of materials that have a lower specific gravity (i.e. hypobaric materials), Kim does not explicitly identify these materials, but common sense would lead the ordinary skilled artisan to consider air, because air is a gas, and gases are less dense and necessarily have a lower specific gravity than water and the CSF. For example, air, which is well known to be a mixture of nitrogen, oxygen, and other gases, is known to have a density of 0.012 g/ml. Thus, air would have a specific gravity of less than 1.0063 (i.e. 0.012) and it would have been prima facie to include air within Soon-Shiong's dispersion systems as modified by the teachings of Kim to obtain a dispersion system that is hypobaric (i.e. has a specific gravity value lower than the specific gravity of the CSF). An ordinary skilled artisan would have had a reasonable expectation of modifying Soon-Shiong's teachings per the teachings and suggestions of Kim, because it was known to include materials to adjust the specific gravity of dispersion systems relative to the specific gravity of the CSF (Kim).

Furthermore, regarding the recited specific gravity ranges, Applicants have identified vegetable oils as having a specific gravity that is less than 1.0063. Because the term about has not been defined, it is the Examiner's position that a specific gravity of "about 1.0063", regardless of whether the recited specific gravity is indicated as being greater than or less than, would necessarily include values above and below 1.0063. Thus, vegetable oil would necessarily have a specific gravity of "about 1.0063." Regarding the incorporation of PEG (polyethylene glycol), it would have been prima facie obvious to include PEG. Regarding claims 51-52, because Soon-Shiong teaches that the particles may contain fat-soluble vitamins as the active ingredient (e.g. Vitamin E), most of these vitamins are oils, and that the dispersing agent may be removed, Soon-Shiong's teachings impliedly suggest biodegradable particles containing an oil that would act as both a buoyancy agent and a therapeutic agent when administered to the CSF.

Regarding the active agents, it is noted that "cancer" reads on a central nervous system disorder, as evidenced by Applicants' claim 28. Anti-cancer agents, such as taxol, read on the term "neuroprotective agent" as defined by Applicants in paragraph [0024] (i.e. "neuroprotective agent" refers to drugs which alleviate a symptom of or prevent damage to the brain or spinal cord"), because an anti-cancer agent would prevent further damage to the brain or spinal cord caused by cancer as well as treat symptoms caused by the cancer. Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because the combined teachings of the prior art is fairly suggestive of the claimed invention.

Response to Arguments

Applicant's arguments with respect to claims 22-30, 40-45, 47-50, and 52-54 have been considered but are moot in view of the new ground(s) of rejection.

Claims 31 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Soon-Shiong et al. (U.S. Patent No. 5,560,933) ("Soon-Shiong") in view of Kim et al. (WO 94/26250) (New IDS reference) and Harris, D.C. ("Quantitative Chemical Analysis, 4th ed., W. H. Freeman and Co.: 1995, pp 26), as applied to claims 22-30, 40-45, 47-50, and 52-54 above, and further in view of Russell et al. (*Bone Marrow Transplantation*, 1999, *24*, pp 1177-1183) (already of record) and Vook et al. (US 2003/0129233).

Applicant Claims

Applicants claim method as described above, wherein the biodegradable polymer is poly(lactide-co-glycolide) (PLGA) and in some embodiments the active agent consists of living cells selected from bone marrow cells (e.g. red blood cells), fetal neural cells, or stem cells.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

The teachings of Soon-Shiong have been set forth above in the instant office action and are herein incorporated by reference. The teachings of Russell were set forth in the office action mailed 6/2/06 and are restated herein. Russell is provided herein to demonstrate that living cells, specifically bone marrow stem cells and blood cell stem cells, are art recognized therapeutic

agents used in the treatment of leukemia. Leukemia is a kind of cancer and living cells are clearly substantially water insoluble active agents.

Russell teaches comparative studies of the treatment of patients with acute myelogenous leukemia (AML) and Myelodysplasia (MDS) who received sibling transplants **with stem cells** from peripheral blood (blood cell transplant, BCT) or bone marrow (BMT). Russell concluded by stating that while disease-free survival may be better using BCT than BMT for AML, it may greatly impair quality of life, due to a higher proportion of acute graft-versus-host disease (GVHD) (abstract).

Vook teaches particularly effective compositions for the localized delivery of chemotherapeutic hydrophobic anticancer agents, inclusive of **paclitaxel (taxol)**, doxorubicin, 5-fluorouracil, campthothecin, cisplatin, and metronidazole, their corresponding derivatives and functionally equivalents, and combinations thereof from **PLGA microspheres** [0006]. Vook's invented PLGA/Taxol microspheres afford controlled/sustained release of taxol and offer many clinical advantages, such as (1) improved patient compliance, as the number of drug dosings are decreased because the depot contains an amount of drug equivalent to multiple doses; (2) isolation depot from the tissue via its incorporation in PLGA thus reducing the drug concentration exposed to the one time and decreasing the chance of tissue injury of the drug copolymer, tissue at any at the depot site; (3) controlled drug release, which may allow for increased dosages of hydrophobic drugs to be administered without systemic toxicity complications. In terms of specific clinical applications of this technology, hydrophobic drug/PLGA formulations are envisioned to play a role in the treatment regiment of cancer and of infection [0287].

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Soon-Shiong lacks the teaching of an intrathecal administration method, wherein the active agent consists of living cells. This deficiency is cured by the teachings of Russell. Soon-Shiong lacks the teaching of an intrathecal administration method, wherein the biodegradable polymer is PLGA. This deficiency is cured by the teachings of Vook.

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been prima facie obvious to modify the teachings of Soon-Shiong to substitute taxol for bone marrow stem cells or red blood stem cells, because both bone marrow stem cells or red blood stem cells have been shown as being suitable for treating leukemia a kind of cancer and taxol is a known anti-cancer agent. Furthermore, it would have been prima facie obvious to substitute taxol for bone marrow stem cells or red blood stem cells to treat leukemia, a kind of cancer, because both taxol and bone marrow stem cells or red blood stem cells are known to be suitable for the treatment of cancer. An ordinary skilled artisan would have been motivated to utilize bone marrow stem cells or red blood stem cells as the active agent in Soon-Shiong's invented compositions, because bone marrow stem cells or red blood stem cells are clearly substantially water insoluble active agents. An ordinary skilled artisan would have had a reasonable expectation of success upon incorporation of bone marrow stem cells or red blood stem cells into Soon-Shiong's invented compositions, because bone marrow stem cells or red blood stem cells are substantially water insoluble active agents. Regarding the use of PLGA as the biodegradable polymer shell, this would have been prima facie obvious, because PLGA is a

well-known conventional biocompatible and biodegradable polymer. An ordinary skilled artisan would have been motivated to modify Soon-Shiong's teachings and utilize PLGA/taxol microspheres, because PLGA/taxol microspheres are conventional compositions used to deliver taxol, are reasonable expected to enhance patient compliance due to the controlled/sustained release properties of the PLGA/taxol microspheres, and taxol is isolated from the body in the PLGA microsphere and, thus, less likely to induce tissue damage. An ordinary skilled artisan would have had a reasonable expectation of modifying Soon-Shiong's teachings to utilize PLGA as the polymer shell and obtain suspensions wherein the polymer shells contained taxol suspended in a dispersing agent (e.g. vegetable oil) and deliver the resulting composition intrathecally, because Soon-Shiong's compositions are suitable for intrathecal administration and taxol/PLGA are well known compositions. Thus, an ordinary skilled artisan would have been motivated to utilize Soon-Shiong's invented composition modified to contain bone marrow or red blood stem cells in to treat cancer via intrathecal administration with a reasonable expectation of success.

Response to Arguments

Applicant's arguments with respect to claims 22-30, 40-45, 47-50, and 52-54 have been considered but are moot in view of the new ground(s) of rejection.

Allowable Subject Matter

Claims 46 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. The art of record does not suggest the preparation of biodegradable

polymer particles containing therein a therapeutic agent in combination with a hydrofluorocarbon.

Conclusion

Claims 22-31, 39-45, 47-50, and 52-54 are rejected. Claim 46 is objected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Alstrum-Acevedo whose telephone number is (571) 272-5548. The examiner is on a flexible schedule, but can normally be reached on M-F ~10am~5:30 pm, and Saturdays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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